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TRANSMITTAL OF APPEAL BRIEF (Large Entity)

Docket No.  
12.026011 DIV

In Re Application Of: Hung et al

Application No.	Filing Date	Examiner	Customer No.	Group Art Unit	Confirmation No.
10/622,743	07-21-03	Sang, Hong	0000 38732	1643	4720

Invention: Identifying Materials from a Breast Duct



COMMISSIONER FOR PATENTS:

Transmitted herewith is the Appeal Brief in this application, with respect to the Notice of Appeal filed on:  
January 29, 2007

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Dated: 6/5/2007

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PATENT

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of:	)	
	)	Examiner: Sang, Hong
David HUNG	)	
	)	Group Art Unit: 1643
Serial No. 10/622,743	)	
	)	
Filed: July 21, 2003	)	Attorney Docket No.: 12.026011 DIV
	)	
For: IDENTIFYING MATERIALS FROM	)	
A BREAST DUCT	)	
	)	

Commissioner for Patents  
Washington, DC 20231

June 5, 2007

**APPEAL BRIEF**

Sir:

This Appeal Brief is filed pursuant to the "Notice of Appeal to the Board of Patent Appeals and Interferences" filed January 29, 2007.

**Real Party in Interest.**

The real party in interest in this appeal is Cytoc Corporation, Inc., the assignee of the above-referenced patent application.

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**Related Appeals and Interferences.**

There are no related appeals and/or interferences involving this application or its subject matter.

**Status of Claims.**

Claims 13, 14, 17, 25, 26 and 29 are the subject of this appeal. The claims appear in Appendix A. Claim 18 is dependant upon a previously canceled claim (claim 16) and should have been canceled in the response mailed September 8, 2006. For the purpose of clarity, claim 18 is not included in this appeal. Claims 1-12, 15-16, 19-24, 27-28, and 30-40 have been cancelled.

**Status of Amendments.**

All of Appellants' amendments have been entered.

**Summary of Claimed Subject Matter.**

The pending claims of the present invention are directed to methods and systems for identifying material from a breast duct using one or more markers that can be identified in ductal fluid retrieved from the breast. A summary of the invention may be found at pages 3-4, in particular, lines 17-35 on page 4 of the specification.

**Grounds of Rejection to be Reviewed on Appeal.**

Issue--Whether claims 13, 14, 17, 25, 26 and 29 are patentable under 35 U.S.C. 103(a) over JAMA (1973, 224(6):823-827) in view of Love *et al.* (Lancet 1996, 348:997-999), Hou *et al.* (Radiology, 1995, 195(2): 568-569) and U.S. Patent No. 6,287,790.

## **ARGUMENT**

***Whether claims 13, 14, 17, 25, 26 and 29 are patentable under 35 U.S.C. 103(a) over JAMA (1973, 224(6):823-827) in view of Love et al. (Lancet 1996, 348:997-999), Hou et al. (Radiology, 1995, 195(2): 568-569) and U.S. Patent No. 6,287,790.***

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or combined references) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on Appellants' disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Independent claim 13 recites a method for identifying a patient having breast cancer or breast precancer comprising placing a ductal access tool comprising a single lumen in a breast duct of a patient; infusing a fluid into the duct through the single lumen; retrieving a ductal fluid sample from the accessed duct through the single lumen; and examining the ductal fluid sample to determine the presence of a marker comprising an expression product of a gene encoding a nuclear matrix protein. The named inventors of the present application are some of the pioneers in the field of ductal lavage, a method by which a small catheter is used to introduce fluid into a breast duct for the purpose of collecting cells for further examination.

Claim 13 and those claims which depend therefrom (14, 17, 25, 26 and 29) remain rejected as unpatentable under 35 U.S.C. 103(a) over JAMA (1973, 224(6):823-827) (hereinafter referred to as "Sartorius") in view of Love *et al.* (Lancet 1996, 348:997-999) (hereinafter referred to as Love), Hou *et al.* (Radiology, 1995, 195(2): 568-569) (hereinafter referred to as Hou) and U.S. Patent No. 6,287,790 issued to Lelievre, *et al.* (hereinafter referred to as Lelievre). The Examiner has argued that both Sartorius and Love teach the use of a catheter to introduce a wash fluid to a breast duct, collecting washings from the ducts, analyzing the washings and determining the presence of cancer cells or precancerous cells by detecting markers. (Final Office Action page 7). The Examiner has also argued that the catheters of Sartorius and Love comprise a single lumen. While neither Sartorius nor Love teach retrieving ductal wash fluid from the accessed duct through the lumen of a catheter, the Examiner argued that these deficiencies are overcome by the teaching found in Hou. The Examiner has also previously argued that Hou teaches a method of infusing a small volume of sterile water soluble contrast material into a breast duct and then aspirates the solution from the duct through the catheter (June 20, 2006 Office Action at page 8). Therefore, the Examiner concluded that it would have been *prima facie* obvious and one skilled in the art would have been motivated, in view of the teachings of Hou, to modify the method of Love to introduce and retrieve a wash fluid through a lumen of a catheter because Love wanted but failed to do so and Hou has overcome Love's technical difficulties (Final Office Action page 8). The Appellants respectfully disagree that the Examiner has established a *prima facie* case of obviousness.

**I. There is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings.**

To establish a *prima facie* case of obviousness, it is necessary for the Examiner to present evidence, preferably in the form of some teaching, suggestion, incentive or inference in the applied references, or in the form of generally available knowledge, that one having ordinary skill in the art would have been motivated to make the claimed invention. See, e.g., *Carella v. Starlight Archery*, 804 F.2d 135, 231 USPQ 644 (Fed. Cir. 1986); and *Ashland Oil, Inc. v. Delta Resins and Refractories, Inc.*, 776 F.2d 281, 227 USPQ 657 (Fed. Cir. 1985).

A new combination of elements can be patented “whether it be composed of elements all new, partly new or all old.” *Rosmount, Inc. v. Beckman Instruments, Inc.*, 727 F.2d 1540, 1546, 221 USPQ 1, 7 (CAFC 1984). The Court of Appeals for the Federal Circuit has forcefully stated that a claim rejection must provide a specific motivation in the art for combining elements from cited art in order to establish obviousness of a new combination.

“[C]ase law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references. ... Combining prior art references without evidence of such a suggestion, teaching, or motivation simply takes the inventor’s disclosure as a blueprint for piecing together the prior art to defeat patentability--the essence of hindsight. ... [Evidence of a suggestion, teaching, or motivation to combine] must be clear and particular. ... Broad conclusory statements regarding the teaching of multiple references, standing alone, are not ‘evidence.’ ... [A] reference-by-reference, limitation-by-limitation analysis fails to demonstrate how the [cited]

references teach or suggest their combination ... to yield the claimed invention," and a conclusion of obviousness based on such an analysis "as a matter of law, cannot stand." *In re Dembiczak*, 175 F.3d 994, 999, 1000, 50 USPQ2d 1614, 1617, 1618 (Fed. Cir. 1999), emphasis added.

*Dembiczak* involved patent claims to "a large trash bag made of orange plastic and decorated with lines and facial features, allowing the bag, when filled with trash or leaves, to resemble a Halloween-style pumpkin, or jack-o'-lantern." *Dembiczak*, 996, 1616. The prior art cited by the Board included: a book describing how to teach children to make a "Crepe Paper Jack-O-Lantern;" a book describing a method of making a "paper bag pumpkin" by stuffing a bag with newspapers, painting it orange, and then painting on facial features with black paint; a U.S. Patent describing a bag apparatus wherein the bag closure is accomplished by the use of folds or gussets in the bag material; design patents issued to *Dembiczak*; and prior art "conventional" plastic lawn or trash bags. The Federal Circuit held that the claimed pumpkin-style trash bag was not obvious because there was no clear, particular motivation to combine the cited references.

This holding of *Dembiczak* that evidence of motivation to combine must be clear and particular to establish obviousness has been emphasized over and over again by the Federal Circuit since *Dembiczak* was decided. It was strongly reemphasized in *Ruiz v. A.B. Chance Co.*, 57 USPQ2d 1161 (Fed. Cir. 2000):

In order to prevent a hindsight-based obviousness analysis, we have clearly established that the relevant inquiry for determining the scope and content of the prior art is whether there is a reason, suggestion, or motivation in the prior art or elsewhere that would have led one of ordinary skill in the art to combine the references. See, e.g., *In re Rouffet*, 149 F.3d 1350, 1359, 47 USPQ2d 1453, 1459 (Fed. Cir. 1998) ("[T]he Board must identify specifically . . . the reasons one of ordinary skill in the art would have been motivated to select the references and to combine them to render the claimed invention obvious."); In

re Dembiczak, 175 F.3d at 999, 50 USPQ2d at 1617 ("Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references."). "Determining whether there is a suggestion or motivation to modify a prior art reference is one aspect of determining the scope and content of the prior art, a fact question subsidiary to the ultimate conclusion of obviousness." Sibia Neurosciences, Inc. v. Cadus Pharma. Corp., 225 F.3d 1349, 1356, 55 USPQ2d 1927, 1931 (Fed. Cir. 2000); Tec Air, Inc. v. Denso Mfg., Inc., 192 F.3d 1353, 1359, 52 USPQ2d 1294, 1298 (Fed. Cir. 1999) (stating that the factual underpinnings of obviousness include whether a reference provides a motivation to combine its teachings with those of another reference).

... there is "a general rule that combination claims can consist of combinations of old elements as well as new elements," Clearstream Wastewater Sys. v. Hydro-Action, Inc., 206 F.3d 1440, 1446, 54 USPQ2d 1185, 1189-90 (Fed. Cir. 2000), "[t]he notion . . . that combination claims can be declared invalid merely upon finding similar elements in separate prior patents would necessarily destroy virtually all patents and cannot be the law under the statute, § 103." Panduit Corp. v. Dennison Mfg. Co., 810 F.2d 1561, 1575, 1 USPQ2d 1593, 1603 (Fed. Cir. 1987); Arkie Lures, Inc. v. Gene Larew Tackle, Inc., 119 F.3d 953, 957, 43 USPQ2d 1294, 1297 (Fed. Cir. 1997) ("It is insufficient to establish obviousness that the separate elements of the invention existed in the prior art, absent some teaching or suggestion, in the prior art, to combine the elements."). *Ruiz* at 1167

Applying this standard to the references cited by the Examiner, it is clear that the Examiner has failed to meet the burden of providing evidence of a motivating force sufficient to impel a person of ordinary skill in the art to combine the teachings in the applied references in the proposed manner to arrive at the claimed invention. The motivation cited in the Office Action for the proposed combination is as follows:

"Therefore, it would have been prima facie obvious and one skilled in the art would have been motivated, in view of the teachings of Hou, to modify the method of Love to introduce and retrieve a wash fluid through a lumen of a catheter because Love wanted but failed to do so and Hou has overcome Love's technical difficulties."



(November 7, 2005 Final Office Action, page 8.) This statement does not provide the clear, particular suggestion in the art for making the specific claimed combination as is required. The Examiner has failed to meet the burden of providing evidence of a motivating force sufficient to impel a person of ordinary skill in the art to combine the teachings of Sartorius, Love, Hou, or Lelievre to arrive at the claimed invention.

Love describes a method of using endoscopy to study stages of cancerous breast disease. The Examiner argued that Love teaches the collecting of ductal fluid from a breast comprising inserting a cannula into one or more breast ducts, infusing saline into the breast ducts, collecting the washings from the ducts and analyzing the washings cytologically. Hou teaches a method of duct cannulation for galactography before excision of a patient's breast. Hou does not teach or suggest the use of a single lumen catheter to introduce and remove wash fluid from a breast duct for the purpose of analyzing the contents of the wash solution. The Examiner argued that one skilled in the art would have been motivated, in view of the teachings of Hou, to modify the method of Love to introduce and retrieve a wash fluid through a lumen of a catheter because Love wanted but failed to do so and Hou has overcome Love's technical difficulties (Final Office Action page 8). The Appellants respectfully disagree.

It is difficult to imagine that one skilled in the art would look to Hou to overcome the technical difficulties of Love. First, although both Hou and Love use the same technical procedure of cannulating a breast duct, Hou was not concerned with the removal of fluid from the breast duct for the analysis of cancer markers. Hou merely describes the removal of fluid containing contrast agent from a breast duct after the successful completion of a mammogram

(page 568; third column). One skilled in the art would have no motivation to look towards Hou as teaching a method of removing cells from a breast duct. Second, the Examiner has not pointed out with any specificity to any teaching or suggestion in Hou that overcomes Love's technical difficulties. Again, since Hou describes a method for ductal cannulation for galactography, the technical difficulties described in Love relating to the remove of fluid from the breast duct was never a concern and was therefore never contemplated by the teaching of Hou. Lastly, the Examiner has not argued with any specificity what exactly Hou teaches to overcome the technical limitations of Love. There is no discussion in Hou of any change or modification of the methodology to overcome a technical difficulty. The Appellants would argue that without such a teaching or suggestion, the Examiner has failed to meet the burden of providing evidence of a motivating force sufficient to impel a person of ordinary skill in the art to modify the method of Love to introduce and retrieve a wash fluid through a lumen of a catheter.

The Appellants respectfully submits that the Examiner has, at most, set forth an "obvious to try" rationale in support of this obviousness rejection. However, an "obvious to try" rationale is not the appropriate standard for obviousness under 35 U.S.C. §103 (M.P.E.P. §2145). In view of the foregoing, Appellants respectfully submit that Love and Hou either alone or in combination, fail to teach a method for identifying a patient having breast cancer or breast precancer comprising placing a ductal access tool comprising a single lumen in a breast duct of a patient; infusing a fluid into the duct through the single lumen; retrieving a ductal fluid sample from the accessed duct through the single lumen; and examining the ductal fluid sample to determine the presence of a marker comprising an expression product of a gene encoding a

nuclear matrix protein as recited in the claims. Accordingly, Appellants respectfully request reconsideration and withdrawal of the rejection of claims 13, 14, 17, 25, 26 and 29 under 35 U.S.C. 103(a).

## **II. There is no reasonable expectation of success.**

Under section 103(a), "[b]oth the suggestion and the expectation of success must be founded in the prior art, not in Appellant's disclosure" (*Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.* 927 F.2d 1200, 1207, 18 USPQ2d 1016 (Fed.Cir. 1991), quoting *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed Cir. 1988)). Appellants believe that the Examiner has failed to establish a *prima facie* case of obviousness since and either alone or in combination, failed to provide the necessary expectation of success for the ordinarily skilled artisan to arrive at the claimed invention.

The references describe methods of cannulating breast ducts for galactography and endoscopy. There would be no expectation that such methods would be successfully used to place a ductal access tool comprising a single lumen in a breast duct of a patient; infusing a fluid into the duct through the single lumen; retrieving a ductal fluid sample from the accessed duct through the single lumen; and examining the ductal fluid sample to determine the presence of a marker. One of the advantages of method of the present invention is the ability to access and retrieve fluid containing cellular material from a breast duct through a single lumen catheter.

While neither Sartorius nor Love teach retrieving ductal wash fluid from the accessed duct through the lumen of a catheter, the Examiner has argued that these deficiencies are

overcome by the teaching found in Hou. The Examiner has also previously argued that Hou teaches a method of infusing a small volume of sterile water soluble contrast material into a breast duct and then aspirates the solution from the duct through the catheter. Even assuming *arguendo* that Hou teaches a method of removing fluid from a breast duct, there is no expectation that the use of the single lumen catheter described in Hou would work in the method of Love.

Love describes a method of cannulating a breast duct and the addition of wash fluid into said ducts. Love then goes on to describe attempts to remove the fluid from the breast ducts. In particular, Love describes that "...the duct is so small that it is difficult to aspirate back through a cannula to obtain material." (results section; fifth paragraph) In fact, Love mentions that washings were not collected by aspirating back through a cannula but during washing "...we remove the catheter and collect the fluid externally in a capillary tube." Thus, in fact, Love teaches away from the use of a catheter to remove ductal washings. In the Final Office Action of November 7, 2006, the Examiner disagreed, arguing that "...while Love teaches that it is difficult to aspirate back through the cannula to obtain material", Love also teaches that "...collecting washings externally after removing the catheter is not optimal and other methods such as a double-lumen tube is being developed too overcome this difficulty. Therefore, the teachings of Love suggest that retrieving the ductal washings through a lumen is a preferred method to collecting the washings externally." (page 7-8)

The Appellants disagree that the teaching in Love of retrieving ductal washings through a lumen is a preferred method let alone the use of a single lumen catheter to retrieve ductal fluid as required by the claims of the current invention. Love clearly demonstrates the difficulty of using

a single lumen catheter to aspirate ductal fluid from a breast duct. To overcome this technical problem, the authors suggested that a double lumen catheter might overcome the problems; however, there is nothing in Love that would teach one of skill in the art that such a modification would overcome the technical problem. The Examiner's argument that the teachings of Love suggest that retrieving the ductal washings through a lumen is a preferred method to collecting the washings externally is not supported by the evidence and the use of a single lumen catheter is clearly unsupported by the teaching of Love. Hou does not overcome the deficiencies of Love because the use of a single lumen catheter in Hou does not address the technical problems that Love encountered. The Examiner has not provided any argument of why the single lumen catheter that did not work in Love could be successfully substituted by the single lumen catheter in Hou.

Appellants believe that the Examiner has failed to establish a *prima facie* case of obviousness since neither Love nor Hou alone or in combination, fail to provide the necessary expectation of success for the ordinarily skilled artisan to arrive at the claimed invention. Accordingly, Appellants respectfully request reconsideration and withdrawal of the rejection of claims 13, 14, 17, 25, 26 and 29 under 35 U.S.C. 103(a).

**III. The prior art reference (or combined references) do not teach or suggest all the claim limitations**

To establish a *prima facie* case of obviousness includes the criteria that all of the limitations of the claims must be taught or suggested by the prior art. *In re Royka* 490 F.2d 981 (C.C.P.A. 1974). Since, under the obviousness standard, the prior art must teach or suggest all the limitations of the claims, then it is axiomatic that non-enabling disclosures should not be considered prior art (See *e.g.*, *In re Wilder*, 429 F.2d 447, 166 USPQ 545, 548 (C.C.P.A. 1970).

Appellants respectfully traverse the rejection that claims 13, 14, 17, 25, 26 and 29 are obvious over Sartorius in view of Love, Hou, and Lelievre on the grounds that the Examiner has failed to establish a *prima facie* case of obviousness, since Sartorius, Love, Hou, or Lelievre either alone or in combination, fail to teach or suggest the claimed invention.

The Examiner argued that both Sartorius and Love teach use of a catheter to introduce a wash fluid to a breast duct, collecting washings from the ducts, analyzing the washings and determining the presence of cancer cells or precancer cells by detecting markers such a reverse transcriptase (Final Office Action; page 7). The Examiner also argued that the catheters of Sartorius and Love comprise a single lumen (Final Office Action; page 7). The Appellants respectfully disagree.

Sartorius does not teach or suggest all of the limitations of the present claims including the use of a single lumen catheter to remove fluid from a breast duct as well as determining the presence of a marker in a fluid sample. Love does not teach or suggest the use of a single lumen

catheter to introduce and remove wash fluid from a breast duct. As mentioned previously, Love teaches away from the use of a catheter to remove ductal washings because as stated in Love “...the duct is so small...that it is difficult to aspirate back through the cannula to obtain material. When washing, we removed the catheter and collect the fluid externally in a capillary tube.” (page 998, 2<sup>nd</sup> paragraph). In the Final Office Action of November 7, 2006, the Examiner argued that Love does not teach away from the instant invention but instead, the teachings of Love suggest that “...retrieving the ductal washings through a lumen is a preferred method to collecting the washings externally.” (page 7-8) Again, as argued previously, the Appellants disagree that the teaching in Love of retrieving ductal washings through a lumen is a preferred method let alone the use of a single lumen catheter to retrieve ductal fluid as required by the claims of the current invention. Love clearly demonstrates the difficulty of using a single lumen catheter to aspirate ductal fluid from a breast duct. The Examiner’s argument that the teachings of Love suggest that retrieving the ductal washings through a lumen is a preferred method to collecting the washings externally is not supported by the evidence and the use of a single lumen catheter is clearly unsupported by the teaching of Love. Thus, Love does not teach or suggest the use of a single lumen catheter to introduce and remove wash fluid from a breast duct, as well as examining the ductal fluid sample to determine the presence of a marker. Love also does not teach or suggest examining the ductal fluid sample to determine the presence of a marker.

The Examiner argued that these deficiencies are made up for in the teachings of Sartorius, Love, Hou, and Lelievre. In particular, the Examiner states that a person of ordinary skill in the art would have been motivated to combine the teachings Sartorius, Love, Hou, and Lelievre

because "...[Sartorius] and Love teach method of diagnosing breast cancer by isolating a ductal fluid from one or more breast ducts by ductal lavage and further detecting a cancer marker in the isolated ductal fluid, Hou teaches retrieving the solution from the duct through the catheter and [Lelievre] teaches that NuMA is a breast cancer marker that can be used to identify breast tumor cells and different stages in the breast tumor progression and differentiation processes." The Appellant disagrees.

First, neither Sartorius nor Love teach or suggest a method of introducing and retrieving a sample from a breast duct via a single lumen catheter. In fact, Love specifically teaches that the use of a single lumen catheter does not work when trying to aspirate a sample back through a catheter disposed within a duct of a breast and thus a different methodology had to be used to obtain a sample. The Examiner suggests that such a deficiency may be made up by Hou. The Appellants disagree. Hou does not teach or suggest the introduction and retrieval of a ductal lavage solution from a duct through a catheter. Hou teaches a method for introducing a dye into a breast duct solely for the purpose of galactography. Once the dye has been introduced and the galactography procedure is finished, the dye is removed and discarded. There is nothing in Hou that teaches or suggests that the dye removed from the duct after the procedure is over contains any cellular material or markers that would be useful in detecting cancer or precancer.

Second, neither Sartorius nor Love teach or suggest detecting the presence of a cancer marker in the isolated ductal fluid. Sartorius mentions that the testing for elevated levels of the enzyme reverse transcriptase may be implicated as a possible cancer marker. Thus, the presence of reverse transcriptase in a fluid sample is used in Sartorius to classify women who are at "high



risk” of getting breast cancer. As mentioned in Sartorius, women who use oral contraceptives have high titers of reverse transcriptase but they do not necessarily have cancer. Thus, the “marker” used in Sartorius is not used to determine the presence of cancer in a patient. In the Final Office Action, the Examiner argued that “...the fact that the marker of Sartorius cannot be used to diagnose a subpopulation (women who use oral contraceptives) for the presence of breast cancer does indicate it would not be a diagnosis marker because no diagnosis marker or treatment is perfect and suitable for any and all populations.” (page 9) The Appellant disagrees. The Appellant would argue that Sartorius does not teach the examining of a ductal fluid sample to determine the presence of a marker. Because young women who take oral contraceptives also have high concentrations of reverse transcriptase, Sartorius is at best ambiguous as to whether or not the presence of high amounts of reverse transcriptase is a cancer marker in breast ductal fluid. As stated by Dr. Sartorius in the article “What this means we just don’t know at the moment.” (page 827; second column). Thus, Sartorius cannot be relied upon by the Examiner to teach the presence of cancer markers in isolated ductal fluid. Appellant respectfully submits that the Examiner has, at most, set forth an “obvious to try” rationale in support of this obviousness rejection. However, an “obvious to try” rationale is not the appropriate standard for obviousness under 35 U.S.C. §103 (M.P.E.P. §2145).

The same holds true for Love. Love uses positive membrane neu immunoreactivity, positive nuclear p53 immunoreactivity or aneuploidy to confirm a previous diagnosis of DCIS. The “markers” as taught in Love were not used for identifying a patient having breast cancer or breast precancer. Thus, the Examiner’s argument that Sartorius and Love teach method of

diagnosing breast cancer by isolating a ductal fluid from one or more breast ducts by ductal lavage and further detecting a cancer marker in the isolated ductal fluid is not supported by the evidence.

Lastly, Lelievre does not teach or suggest that NuMA is a breast cancer marker that can be used to identifying a patient having breast cancer or breast precancer. Lelievre teaches the use of NuMA as a marker for examining the different stages in the breast tumor progression. There is simply no teaching or suggestion in Lelievre that NuMA could be used as a diagnostic marker for the presence of cancer. Thus, the Examiner's argument that NuMA is a breast cancer marker that can be used to identify breast tumor cells is not supported by the evidence. Lelievre teaches the localization of nuclear apparatus proteins (NuMA) to identify tumor cells and different stages in the tumor progression and differentiation processes. Lelievre does not teach or suggest that the presence of NuMA in a ductal fluid sample can be used as a marker for determining a cancerous or precancerous condition in the breast of a patient. Lelievre mere examines the localization of NuMA within cell lines.

In view of the foregoing, Appellants respectfully submit that Sartorius, Love, Hou, and Lelievre, alone or in combination, fail to teach or suggest a method for identifying a patient having breast cancer or breast precancer comprising placing a ductal access tool comprising a single lumen in a breast duct of a patient; infusing a fluid into the duct through the single lumen; retrieving a ductal fluid sample from the accessed duct through the single lumen; and examining the ductal fluid sample to determine the presence of a marker comprising an expression product of a gene encoding a nuclear matrix protein, as recited in the claims. The obviousness rejection

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is based on hindsight from these disparate references to provide random elements of the claims. There is no clear, particular motivation in the references to reach the claimed invention. Prima facie obviousness has not been established under such conditions. Accordingly, Appellants respectfully request reconsideration and withdrawal of the rejection of claims 13, 14, 17, 25, 26 and 29 under 35 U.S.C. § 103(a).

### CONCLUSION

In view of the arguments presented above, the Appellant contend that each of claims 13, 14, 17, 25, 26 and 29 are patentable. Therefore, reversal of the rejections under 35 U.S.C. §103(a) is respectfully solicited.

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Respectfully submitted,



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## **APPENDIX A: APPEALED CLAIMS**

13. A method for identifying a patient having breast cancer or breast precancer, said method comprising;

placing a ductal access tool comprising a single lumen in a breast duct of a patient;

infusing a fluid into the duct through the single lumen;

retrieving a ductal fluid sample from the accessed duct through the single lumen; and

examining the ductal fluid sample to determine the presence of a marker comprising an expression product of a gene encoding a nuclear matrix protein.

14. The method of claim 13 wherein the expression product is a polypeptide.

17. The method of claim 13 wherein the nuclear matrix protein is selected from the group consisting of lamin A, lamin B, lamin C, a peripheral matrix protein, nuclear mitotic spindle apparatus protein (NuMA), Topoisomerase II, and an internal nuclear matrix protein.

25. The method of claim 13 wherein the fluid collected is from a single duct.

26. The method of claim 13 wherein a ductal fluid sample is collected from a plurality of ducts.

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29. The method of claim 13 wherein the single lumen has an inner diameter large enough to retrieve clusters of greater than 10 cells.

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## **APPENDIX B: EVIDENCE**

**NONE**

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**APPENDIX C: RELATED PROCEEDINGS**

**NONE**

**CERTIFICATE OF MAILING BY "EXPRESS MAIL" (37 CFR 1.10)**

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07/21/03

Examiner

Sang, Hong

Customer No.

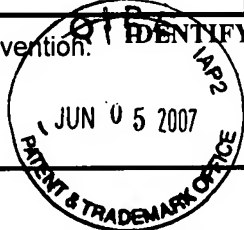
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Group Art Unit

1643

Invention:

IDENTIFYING MATERIALS FROM A BREAST DUCT



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